CLAIMS

1. An attenuated influenza virus carrying a genomic nucleic acid segment which comprises 5' and 3' non-coding regions providing a mutated duplex region of an influenza virus RNA genomic segment operably-linked to a protein coding sequence for an influenza viral protein or a functional modification of said protein, wherein said duplex region is a non-chimeric duplex region, but has at least one base-pair substitution such that expression of said protein-coding sequence in cells infected by said virus is reduced to give an attenuated phenotype.

2. A virus as claimed in claim 1which exhibits a reduction in plaque titre compared to the parent wild-type virus on cells of one or more type selected from Madin-Darby bovine kidney (MDBK) cells, Madin-Darby canine kidney (MDCK) cells and Vero cells.

3. A virus as claimed in claim 2 which exhibits at least about one log reduction in plaque titre compared to the parent wild type virus on MDBK cells.

4. A virus as claimed in claim 2 or claim 3 which exhibits at least about 3 to 4 log reduction in plaque titre compared to the parent wild type virus on MDCK cells and Vero cells.

5. A virus as claimed in any one of claims 1 to 4 wherein said genomic nucleic acid segment is a mutated native influenza virus genomic RNA segment.

6. A virus as claimed in any one of claims 1 to 5 which is an attenuated influenza virus of type A, wherein said nucleic acid segment is a mutated influenza A virus genomic RNA segment having the mutation C to A at position 11 from the 3'-terminus of the native parent segment and the mutation G to U at position 12' from the 5'-terminus of the native parent segment, or functionally equivalent substitutions at the same positions, so as to provide an attenuating base-pair substitution in the non-coding duplex region.

7. A virus as claimed in claim 6 wherein said nucleic acid segment also has the mutation U to G at position 10 from the 3' terminus of the native parent segment and the mutation A to C at position 11' from the 5' terminus of the native parent segment, or functionally equivalent substitutions at the same positions, so as to provide an additional base-pair substitution in the non-coding duplex region.

8. A virus as claimed in claim 6 or claim 7 wherein said nucleic acid segment encodes neuraminidase (NA) or a functional modification thereof.

9. A virus as claimed in any one of claims 1 to 8 which is a wild-type virus which has been attenuated by said base-pair substitution(s).

10. A virus as claimed in any one of claims 1 to 8 which additionally comprises a heterologous coding sequence capable of being expressed in target cells.

11. A virus as claimed in claim 10 wherein said heterologous coding sequence encodes an antigenic peptide or polypeptide capable of stimulating an immune response to a pathogenic agent.

12. A virus as claimed in claim 9 which is attenuated influenza A/WSN/33 having a NA-encoding nucleic acid segment as defined in claim 8.

13. A nucleic acid as defined in claim 1 or any one of claims 5 to 8.

14. A DNA capable of transcription to provide a nucleic acid according to claim 13.

15. A plasmid containing a DNA as claimed in claim 14.

16. A ribonucleoprotein (RNP) complex wherein a nucleic acid as claimed in claim 13 is complexed with polymerase proteins and nucleoprotein of an influenza

virus for use in preparing an attenuated virus as claimed in any one of claims 1 to 12.

17. An *ex vivo* cell infected by a virus as claimed in any one of claims 1 to 12.

18. A vaccine comprising a virus as claimed in any one of claims 1 to 11.

19. A vaccine as claimed in claim 18 which comprises a virus as claimed in claim 11 and which is capable of stimulating an immune response to an influenza virus and a second pathogenic agent other than an influenza virus.

20. A pharmaceutical composition comprising a virus as claimed in claim 10 in combination with a pharmaceutically acceptable carrier or diluent for delivery of said heterologous coding sequence to target cells.

21. A pharmaceutical composition comprising cells infected with a virus according to claim 10 or claim 11 in combination with a pharmaceutically acceptable carrier or diluent.

22. A method of preparing a virus according to any one of claims 1 to 12 which comprises providing in a host cell the genomic nucleic acid segments for said virus under conditions whereby said segments are packaged into a viral particle.

23. Use of a virus as claimed in any one of claims 1 to 12 as a helper virus to rescue an influenza virus genomic nucleic acid segment in cells, wherein viruses produced containing said nucleic acid segment are selected on the basis of increased growth compared with the helper virus on cells of a selected type.

24. Use of an influenza A virus as claimed in claim 8 as a helper virus in accordance with claim 23 to rescue an NA-encoding influenza A virus genomic nucleic acid segment or a functional modification thereof.

25. Use as claimed in claim 24 of attenuated influenza A/WSN/33 having mutations as defined in claim 7 in the NA-encoding genomic RNA segment, wherein selection of viruses carrying the nucleic acid segment to be rescued is carried out on Vero cells.

26. A method of stimulating an immune response against an influenza virus, optionally together with stimulation of an immune response against one or more further pathogenic agents, which comprises administering in an immunising mode an attenuated influenza virus as claimed in any one of claims 1 to 11.

27. A method of delivering a heterologous coding sequence to cells which comprises infecting said cells with a virus according to claim 10 carrying said sequence.